Modeling stochasticity in gene expression: From population models to model populations Internship Offer

Keywords: stochastic processes, gene expression modeling, parameter estimation methods, computational biology, systems biology

1. Supervisor and host laboratory

Supervisor: Gregory Batt, INRIA research scientist within the Contraintes research group at the Paris-Rocquencourt INRIA campus. Work done in collaboration with Pascal Hersen (CNRS, MSC Lab, Paris).

Hosting lab: Contraintes is a research group that aims at developing computational methods and tools to support the analysis and control of natural biological systems and the design and optimization of complex synthetic biology systems. Methodological developments are guided by real-life biological problems defined and studied in close collaboration with experimentalists. This approach ensures the biological relevance of the proposed methods and tools.

2. Context of the internship

Gene expression is a fundamental process by which proteins, the main effectors of cellular processes, are produced. An intriguing open question, raised more than a decade ago, is to understand how cells function in a fairly robust way despite a very significant **stochasticity** in the gene expression process. Indeed genetically-identical cells exposed to the same environmental conditions can show significant variations in molecular content and marked differences in phenotypic characteristics. The joint use of fluorescent gene reporter techniques and microfluidic devices now allows for the **long-term quantitative observation** of gene expression in **single cells**. By using **quantitative modeling and analysis approaches** in combination with this quality data, it is not possible to investigate the aforementioned question in a more precise and formal manner. This should lead to propose molecular mechanisms that are at the core of the stochasticity in the gene expression process.

3. Objectives of the internship

In the context of a project aiming at controlling in real-time gene expression in yeast, we have produced a wealth of quality, long-term gene expression data at the single-cell level. The objective of the

internship is to extend traditional population models to capture two forms of variability: cell-to-cell variability and temporal fluctuations. The first source of variability comes from the fact that, although genetically identical, not all cells behave in the same way. The second source of variability comes from the fact that the physiological state of the cell, among others, evolves with time and this global change indirectly affects the specific gene expression process under study.

As a first step, existing modeling methods will be surveyed to identify those who are adapted to capture these two different but interdependent stochastic aspects, and the associated cost of parameter estimation. In particular we will investigate the possibilities to use a **population of models** rather than a **model of the population**. In a second step, the most promising approaches will be employed and applied to the available data. This should result in a better characterization of the gene expression process in yeast and/or in novel experimental investigations.

4. Candidate profile

We are seeking qualified and motivated applicants with strong skills in applied mathematics and computer science. In particular, the candidate is expected to have a solid background in modeling and analysis of stochastic processes, and an interest for interdisciplinary research. Knowledge in molecular biology will be appreciated.

5. Location and contact details

Location: INRIA Paris-Rocquencourt (near Versailles), in the Contraintes research group. Part of the internship may be carried out at the MSC lab.

Contact: gregory.batt@inria.fr , see also our website at http://contraintes.inria.fr/~batt and http://www.msc.univ-paris-diderot.fr/lab513/